

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method for preventing or treating epithelial tissue damage comprising identifying a patient in need of epithelial tissue protection or treatment, obtaining a substance capable of blocking or modifying endogenous CD₁₄ function that prevents or treats epithelial tissue damage, comprising:

~~a polynucleotide antisense to a sequence comprised by the CD₁₄ gene and or CD₁₄-mRNA;~~

a polynucleotide antisense to a sequence ~~comprised~~ing by the glucosylceramide synthase gene and/or the glucosylceramide synthase mRNA; and administering the substance to said patient.

~~a polynucleotide sense to a sequence comprised by the sphingomyelinase or ceramide synthase gene and/or the sphingomyelinase or ceramide synthase mRNA;~~

~~a polypeptide or peptide, which is not an antibody, binding to CD₁₄ and essentially blocking or modifying CD₁₄ function; and~~

~~a lipid, which is selected from the group consisting of a sterol, fatty acid, glyceride and phosphatidylinositol phosphate.~~

Claim 2 (currently amended): The ~~substance according to method of~~ claim 1, which is a wherein the compound reducing at least one of the reduces transcription and translation of the CD₁₄ gene of the glucosylceramide synthase gene.

Claim 3 (currently amended): The ~~method of substance according to claim 1 which is derived from a source chosen from the group consisting of plants, microbes, animals, ingredients of green tea and carotenoid,~~ wherein the substance is an RNAi oligonucleotide.

Claim 4 (withdrawn): The substance according to claim 1, which is a ligand of a receptor belonging to the TNF super-family.

Claim 5 (withdrawn): A method for the preparation of a carrier for the prevention or treatment of the detrimental effects of stress to epithelial cells and/or hair loss comprising the steps of using a substance capable of blocking or modifying CD_{1d} function selected from the group consisting of:

a polynucleotide antisense to a sequence comprised by the CD_{1d}-gene and or CD_{1d}-mRNA;

a polynucleotide antisense to a sequence comprised by the glucosylceramide synthase gene and/or the glucosylceramide synthase mRNA;

a polynucleotide sense to a sequence comprised by the sphingomyelinase or ceramide synthase gene and/or the sphingomyelinase or ceramide synthase mRNA;

a polypeptide or peptide, which is not an antibody, binding to CD_{1d} and essentially blocking or modifying CD_{1d} function; and

a lipid, which is selected from the group consisting of a sterol, fatty acid, glyceride and phosphatidylinositol phosphate.

Claim 6 (currently amended): A method for preparing a pharmaceutical composition for preventing or treating epithelial tissue damage comprising, containing-obtaining a substance capable of blocking or modifying endogenous CD_{1d} function that prevents or treats epithelial tissue damage, comprising:

~~a polynucleotide antisense to a sequence comprised by the CD_{1d}-gene and or CD_{1d}-mRNA;~~

a polynucleotide antisense to a sequence comprised by the glucosylceramide synthase gene and/or the glucosylceramide synthase mRNA; and combining the substance with a pharmaceutically acceptable carrier.

~~a polynucleotide sense to a sequence comprised by the sphingomyelinase or ceramide synthase gene and/or the sphingomyelinase or ceramide synthase mRNA;~~

~~a polypeptide or peptide, which is not an antibody, binding to CD_{1d} and essentially blocking or modifying CD_{1d} function; and~~

a lipid, which is selected from the group consisting of a sterol, fatty acid, glyceride and phosphatidylinositol phosphate.

Claim 7 (currently amended): The ~~composition according to method of~~ claim 6, which is in a form selected from the group consisting of a food composition, a cosmetic composition and a pharmaceutical composition wherein the substance is an RNAi oligonucleotide.

Claim 8 (currently amended): The ~~composition according to method of~~ claim 6, which is in a form selected from the group consisting of milk, yogurt, curd, cheese, fermented milks, milk based fermented products, ice creams, milk based powders, infant formulae, cereal products, fermented cereal based products, mineral water, chocolate, pet food, lotions, shampoos, creams, sun screens, after sun creams, anti-ageing creams, ointments, tablets, liquid, dried oral supplement, wet oral supplement, dry tube feeding, wet tube feeding and an anti-cancer drug wherein the substance reduces transcription of the glucosylceramide synthase gene.

Claim 9 (withdrawn): A method for the prevention or treatment of damage in epithelial tissues produced by a stress situation comprising the step of administering to an individual a therapeutically-effective amount of a composition comprising a substance capable of blocking or modifying endogenous CD_{1d} function selected from the group consisting of:

a polynucleotide antisense to a sequence comprised by the CD_{1d}-gene and or CD_{1d}-mRNA;

a polynucleotide antisense to a sequence comprised by the glucosylceramide synthase gene and/or the glucosylceramide synthase mRNA;

a polynucleotide sense to a sequence comprised by the sphingomyelinase or ceramide synthase gene and/or the sphingomyelinase or ceramide synthase mRNA;

a polypeptide or peptide, which is not an antibody, binding to CD_{1d} and essentially blocking or modifying CD_{1d} function; and

a lipid, which is selected from the group consisting of a sterol, fatty acid, glyceride and phosphatidylinositol phosphate.

Claim 10 (withdrawn): The method according to claim 9 , wherein the lipid is a phytochemical.

Claim 11 (withdrawn): The method according to claim 9 , wherein the stress situation is selected from the group consisting of a chemical stress, a biological stress and a physical stress.

Claim 12 (withdrawn): The method according to claim 11, wherein the stress is exerted by a situation selected from the group consisting of exposure to oxidants or carcinogens, exposure to bacteria, viruses, fungi, lipids derived from surrounding cells or microbes, or exposure to UV-irradiation.

Claim 13 (withdrawn): The method according to claim 9 , wherein the damage is selected from the group consisting of skin burning, blistering, cataract formation, epidermal hyperplasia, cancer, inflammation, immune suppression, and skin ageing.

Claim 14 (withdrawn): The method according to claim 9 , wherein the epithelial cells are derived from a location selected from the group consisting of the skin, gut, eye, lung, prostate, liver, breast, kidney and the uterus.

Claim 15 (withdrawn): The method according to claim 13 , wherein the cancer is selected from the group consisting of breast cancer, colon cancer, prostate cancer, liver cancer, pancreatic cancer, kidney cancer, non-melanoma and melanoma skin cancers.

Claim 16 (withdrawn): A method for identifying CD₁₄ blocking or modifying substances, comprising the steps of:

- (a) exposing epithelial cells to a substance of interest,
- (b) subjecting the epithelial cells to a stress situation,

- (c) determining the effect of said stress to said epithelial cells by screening for at least one assay selected from the group consisting of,
- (i) epithelial hyperplasia (H&E),
 - (ii) epithelial proliferation (BrUd, PCNA),
 - (iii) epithelial apoptosis (TUNEL),
 - (iv) p53 mutation accumulation,
 - (v) quantitative and qualitative assessment of epithelial lipids,
 - (vi) co-clustering patterns of apoptotic and non-apoptotic cell surface receptors,
 - (vii) production of pro-inflammatory cytokines,
 - (viii) production of immuno-modulatory cytokines,
 - (ix) markers of inflammation,
 - (x) anti-apoptotic transcription factors,
 - (xi) markers of ageing,
- (d) comparing the results obtained with a control.

Claim 17 (withdrawn): The method according to claim 16, wherein the stress situation is selected from the group consisting of a chemical stress, a biological stress and a physical stress.

Claim 18 (withdrawn): The method according to claim 17, wherein the stress is exerted by a situation selected from the group consisting of exposure to oxidants or carcinogens, exposure to bacteria, viruses, fungi, lipids derived from surrounding cells and/or microbes, and by exposure to UV-irradiation.

Claim 19 (withdrawn): The method according to claim 16, wherein the pro-inflammatory cytokines are selected from the group consisting of IL-1, TNF- α , PGE-2, IL-6, IFN- γ and IL-8.

Claim 20 (withdrawn): The method according to claim 16, wherein the immunomodulatory cytokines are selected from the group consisting of PAF, IL-10, IL-4 or TGF- β .

Claim 21 (withdrawn): The method according to claim 16, wherein the lipids are selected from the group consisting of phospholipids, sphingolipids and glycosphingolipids.

Claim 22 (withdrawn): The method according to claim 16, wherein the markers of inflammation include Cox-2 and iNos.

Claim 23 (withdrawn): The method according to claim 16, wherein the anti-apoptotic transcription factors include AP-1 and NFkappaB.

Claim 24 (withdrawn): The method according to claim 16, wherein the markers of aging include elastases, collagenases, metalloproteinases, gelatinases, stromelysins, and telomerases.

Claim 25 (withdrawn): A method for decreasing multi-drug resistance of cancers comprising the steps of administering to an individual taking a cancer drug a therapeutically-effective amount of a composition capable of blocking or modifying endogenous CD_{1d} function selected from the group consisting of:

a polynucleotide antisense to a sequence comprised by the CD_{1d}-gene and or CD_{1d}-mRNA;

a polynucleotide antisense to a sequence comprised by the glucosylceramide synthase gene and/or the glucosylceramide synthase mRNA;

a polynucleotide sense to a sequence comprised by the sphingomyelinase or ceramide synthase gene and/or the sphingomyelinase or ceramide synthase mRNA;

a polypeptide or peptide, which is not an antibody, binding to CD_{1d} and essentially blocking or modifying CD_{1d} function; and

a lipid, which is selected from the group consisting of a sterol, fatty acid, glyceride and phosphatidylinositol phosphate.

Claim 26 (withdrawn): The method according to claim 25, wherein the individual has a cancer selected from the group consisting of skin, gut and breast cancer.

Claim 27 (withdrawn): A method of screening comprising the steps of using cells expressing and/or over-expressing CD₁₄ in an assay for screening for substances modifying and/or blocking CD₁₄ function.

Claim 28 (withdrawn): A method of determining activity of substances comprising the steps of using CD₁₄^{-/-} animals as a test model for determining the activity of substances influencing damages in epithelial tissues produced by a stress situation and/or hair loss.

Claim 29 (withdrawn): A method of providing gene therapy comprising the step of using a substance capable of blocking or modifying endogenous CD₁₄ function selected from the group consisting of:

- a polynucleotide antisense to a sequence comprised by the CD₁₄-gene and or CD₁₄-mRNA;

- a polynucleotide antisense to a sequence comprised by the glucosylceramide synthase gene and/or the glucosylceramide synthase mRNA;

- a polynucleotide sense to a sequence comprised by the sphingomyelinase or ceramide synthase gene and/or the sphingomyelinase or ceramide synthase mRNA;

- a polypeptide or peptide, which is not an antibody, binding to CD₁₄ and essentially blocking or modifying CD₁₄ function; and

- a lipid, which is selected from the group consisting of a sterol, fatty acid, glyceride and phosphatidylinositol phosphate in a gene therapy method.

Claim 30 (withdrawn) The substance according to claim 1, which is a ligand of a receptor belonging to CD95/APO-1/Fas.

Claim 31 (withdrawn): A method for the prevention and/or treatment of hair loss comprising the step of administering to an individual a therapeutically-effective amount of a

substance capable of blocking or modifying endogenous CD_{1d} function selected from the group consisting of:

- a polynucleotide antisense to a sequence comprised by the CD_{1d}-gene and or CD_{1d}-mRNA;

- a polynucleotide antisense to a sequence comprised by the glucosylceramide synthase gene and/or the glucosylceramide synthase mRNA;

- a polynucleotide sense to a sequence comprised by the sphingomyelinase or ceramide synthase gene and/or the sphingomyelinase or ceramide synthase mRNA;

- a polypeptide or peptide, which is not an antibody, binding to CD_{1d} and essentially blocking or modifying CD_{1d} function; and

- a lipid, which is selected from the group consisting of a sterol, fatty acid, glyceride and phosphatidylinositol phosphate.

Claim 32 (withdrawn): The method according to claim 9, wherein the lipid is selected from the group consisting of a natural or synthetic polyphenol, a ginkgolide and vitamin.